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Brief Communication

Respiratory syncytial virus, infants and intensive therapy

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A B S T R A C T

The aims of this study were to determine the presence of respiratory syncytial virus (RSV) and to assess the clinical features of the disease in infants with acute low respiratory tract infection hospitalized at pediatric intensive care units (PICU) of two university teaching hospitals in São Paulo State, Brazil. Nasopharyngeal secretions were tested for the RSV by the polymerase chain reaction. Positive and negative groups for the virus were compared in terms of evolution under intensive care (mechanical pulmonary ventilation, medications, invasive procedures, complications and case fatality). Statistical analysis was performed using the Mann Whitney and Fisher's exact tests. A total of 21 infants were assessed, 8 (38.1%) of whom were positive for RSV. The majority of patients were previously healthy while 85.7% required mechanical pulmonary ventilation, 20/21 patients presented with at least one complication, and the fatality rate was 14.3%. RSV positive and negative groups did not differ for the variables studied. Patients involved in this study were critically ill and needed multiple PICU resources, independently of the presence of RSV. Further studies involving larger cohorts are needed to assess the magnitude of the impact of RSV on the clinical evolution of infants admitted to the PICU in our settings.

Respiratory syncytial virus (RSV) leads to acute lower respiratory tract infection (ALRTI) in approximately 10% of infant cases[1,2] and requires mechanical pulmonary ventilation (MPV) in 7% to 21% of hospitalized patients.[3,4] A review of recent articles retrieved from the Medline database using the search words "Respiratory Syncytial Virus Intensive Therapy Infants" involving different study cohorts showed that newborns and young infants with RSV are at greater risk for MPV, longer hospital stay and higher incidence of complications.[5-14] Although the presence of comorbidities (pneumonia, cardiopathy and prematurity) is associated to poorer evolution, many ICU patients were previously healthy.[5-10] The aims of this study was to determine the presence of RSV and the clinical features of this infection in infants with ALRTI hospitalized in the pediatric intensive care unit (PICU). A prospective descriptive and analytical study was conducted in infants aged between zero and 12 months with ALRTI hospitalized in the PICU of two University teaching hospitals in the Campinas region of São Paulo state, Brazil in 2004, 2007 and 2008. Collection was performed between the months of April and September, a period previously reported to be associated with the highest incidence of the virus in the region.[4,15]

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The inclusion criteria were infants between 0 and 12 months of life and hospitalized in the PICU due to ALRTI. The sole criterion for exclusion was onset of symptoms more than seven days prior to admission.

The diagnosis of ALRTI was reached based on clinical criteria (fever, cough, tachypnea, rales or wheezes on auscultation), supplemented by radiological (hyperinflation, opacities) and gasometric (hypoxemia, hypercapnia, respiratory acidosis) criteria. The combination of these findings determined the need for MPV or otherwise in these patients according to specific medical protocols.[16,17] Nasopharyngeal secretions were collected by aspiration from all patients during the first three days of admission. The material obtained was analyzed by the polymerase chain reaction (PCR) molecular method.[18] Patients were divided into RSV positive and RSV negative groups and assessed for gender, age on admission, previous diseases, length of PICU stay, need for/time on MPV, use of medications, and invasive procedures. During the PICU stay, patients were assessed for prognostic factors of worse evolution on MPV by calculating the ventilation index (VI = peak inspiratory pressure x mechanical respiratory rate/1000) and partial oxygen pressure/fraction of inspired oxygen (PaO_2/FIO_2), and by examining the worse gasometry value of the first day of MPV.[19] Complications were registered after the first day of ICU stay and grouped into cardiologic (myocarditis with cardiac insufficiency or arrhythmias), renal (acute renal insufficiency), neurologic (encephalitis with convulsions and coma), hydroelectrolytic (acidosis, sodium potassium, calcium disturbances), hematologic (anemia, leukopenia, plateletopenia) and respiratory (atelectasis, pleural stroke, pneumothorax) problems.

Data were stored using the Excel program and analysis performed by version 8.2 of the SAS (Statistical Analysis System) software (SAS Institute INC, 1999-2001, Cary, NC, USA). The Mann Whitney and Fisher's exact tests were employed for statistical analysis adopting a significance level of 0.05.

A signed term of informed consent was provided by the guardians of all patients. This project was previously approved by the Research Ethics Committee of the School of Medical Sciences of the Universidade Estadual de Campinas (UNICAMP) under process number 076/2003 and was conducted in accordance with the ethical principles of the World Medical Association and Declaration of Helsinki.

Results given are based on the analysis of 21 infants aged between zero and 12 months hospitalized in the PICU for ALRTI. Regarding patient profile, median age was 2.4 months, 12 subjects were male (52.2%) and eight (38.1%) tested positive on PCR for RSV. Comparison of the RSV-positive and RSV-negative groups by the Mann-Whitney test revealed no difference in the variables age on admission ($p = 0.601$) or length of PICU stay ($p = 0.133$). The majority of patients were previously healthy (57.1%) whereas 9/21 (42.9%) had previous diseases (acquired immunodeficiency, genetic syndromes, cardiopathies). Similarly, the two groups did not differ for previous diseases ($p = 0.200$). A total of 18/21 (85.7%) patients required mechanical pulmonary ventilation during the PICU stay. No difference between the study groups was found for time on ventilatory support ($p = 0.762$, Fisher's exact test), and ventilation index ($p = 0.427$, Mann- Whitney test) or PaO_2/FiO_2 ($p = 0.384$, Mann-Whitney Test). With regard to medication use during PICU stay, no difference was found in use of endovenous corticosteroids, different types of antibiotics, vasoactive drugs or continuous sedation with benzodiazepines or opioids ($p > 0.05$). The patients were underwent a variety of invasive procedures: venous catheter insertion (by deep venipuncture/Intracath®, percutaneous puncture/PICC® and vein dissection/phlebotomy); use of vesical relief and delay probe; chest drainage. In terms of frequency of these procedures, a significant difference was found between groups only for the phlebotomy procedure which was more frequent in RSV-positive patients ($p = 0.042$).

During the PICU stay, 20/21 patients had complications, predominantly respiratory problems (15/21; 71.4%) although no difference between RSV-positive and RSV-negative groups was evident (Table 1). Concerning fatalities, one death occurred in the RSV-positive group and two deaths in the RSV-negative group (3/21, 14.3%), a non-significant difference between the groups ($p = 0.510$, Fisher's exact test). The deaths occurred in young infants that evolved clinically with cardiovascular and infectious complication, one of whom had Down's syndrome. Patient characteristics are shown in Table 2.

Table 1 - Complication types during clinical evolution among infants between zero and 12 months of age hospitalized at the Pediatric Intensive Care Unit for acute lower respiratory tract infection, in respiratory syncytial virus positive and negative groups

Complication	RSV +	RSV -	Total	p*
Cardiologic (myocarditis with cardiac insufficiency or arrhythmias) (yes/no)	1/7	3/10	4/17	0.501
Renal (renal insufficiency) (yes/no)	0/8	1/12	1/20	0.619
Neurological (encephalitis with seizure or coma) (yes/no)	1/7	1/12	2/19	0.628
Hydroelectrolytic (metabolic acidosis, disturbances in sodium, potassium or calcium) (yes/no)	2/6	1/12	3/18	0.315
Hematologic (anemia, leukopenia, thrombocytopenia) (yes/no)	5/3	7/6	12/9	0.527
Respiratory (atelectasis, plural stroke, pneumothorax) (yes/no)	6/2	9/4	15/6	0.590

RSV, respiratory syncytial virus; *p = Fisher's exact test.

Table 2 - Characteristics of patients evolving to death among infants between zero and 12 months of age hospitalized in the Pediatric Intensive Care Unit for acute lower respiratory tract infection

Patient	1	2	3
RSV	Negative	Positive, GA2 genotype	Negative
Gender	Male	Female	Male
Age	3 months	3 months	5 months
ALRTI-associated diagnoses	Acute laryngitis	Wheezing infant	Down syndrome Inter-atrial communication Cardiac insufficiency Hypothyroidism
MPV time	1 day	8 days	12 days
Invasive procedures	None	Central venous puncture (Intracath®) Vesical probe	Central venous puncture (Intracath®) Vesical probe
Vasoactive drugs	None	Dobutamine and dopamine	Dobutamine and noradrenaline
Complications	Pulmonary hypertension	Pulmonary hypertension Hospital-acquired urinary tract infection	Hospital-acquired pneumonia pneumothorax
Corticosteroids	Yes	Yes	Yes
Antibiotics	No	Aminoglycosides	Cephalosporin and aminoglycoside
Cultures	Negative	Negative	Negative
Cause of death	Acute respiratory insufficiency with pulmonary hypertension	Septic shock	Septic shock

ALRTI, acute lower respiratory tract infection; MPV, mechanical pulmonary ventilation.

The overall result of the present study was that clinical pictures among the cohort studied were no more severe in RSV-positive patients than RSV-negative individuals. In the present population, although the proportion of males and the age group were consistent with those of a similar study,[15] RSV-positive and negative patients were comparable in terms of PICU stay, MPV and complications, a finding that contrasts with earlier reports.[6,8,11,14] However, it should be noted that the present study included infants only up to 12 months of age and that the worse evolution seen in RSV-positive patients affected mainly young infants, particularly newborns.[5,8] Another noteworthy point is that comparison of our results with those in the literature was hampered by the fact that the present study included three forms of clinical presentation (bronchiolitis, pneumonia and pneumonia plus bronchiolitis) whereas the majority of earlier studies considered only patients with bronchiolitis.[1,2,16] This broader inclusion was based on results of a previous study involving a large cohort (n = 144) performed in the same hospitals that showed a predominance of the bronchiolitis-plus-pneumonia form among patients hospitalized for RSV.[20] Akin to the findings of other authors,[10] the present cohort comprised patients that were predominantly previously healthy (57.1%). In contrast to other cohorts investigated, the patients with previous diseases in the present study did not have worse evolution.[6,8,11,14] This finding might be explained by the small number of patients included in the study.

In the present study sample patients were critically ill and needed multiple PICU resources, independently of the presence of RSV.

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Conflict of interest

All the authors declare to have no conflict of interest.

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